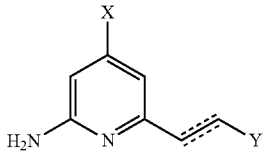
degenerative diseases such as Alzheimer's, Parkinson's, and Huntington's diseases, and amyotrophic lateral sclerosis, cerebral palsy, stroke/ischemic brain damage, and migraine headaches.

[0009] The disclosed compounds include derivatives of 2-aminopyridine. The disclosed compounds may have a formula (I) as follows:

(I)



[0010] where X is hydrogen, C_1-C_6-alkyl (e.g., methyl), C_1-C_6-alkoxy (e.g., methoxy), halogen (e.g., fluoro or chloro), or haloalkyl (e.g., CH_2F, CF_2H, or CF_3),

[0011] ≡ represents a single, double, or triple bond;

[0012] Y is substituted aryl (e.g., substituted phenyl) or substituted heteroaryl (e.g., substituted quinolinyl such as substituted quinolin-3-yl), wherein Y is substituted at one or more ring positions with halogen or a substituent having a formula —Z—R^a and Y optionally is substituted at two or more ring positions with halogen (e.g., 2,3-difluoro-phenyl); or

[0013] Y has a formula —Z—R^a;

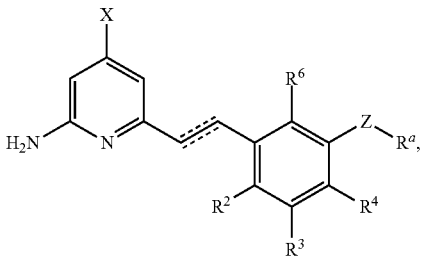
[0014] Z is selected from C_1-C_6-alkyl, C_2-C_6-alkenyl, and C_2-C_6-alkynyl;

[0015] R^a is selected from amino, alkylamino (e.g., methylamino), dialkylamino (e.g., dimethylamino), or a 4-6 membered heterocycle which contains at least one nitrogen atom and which heterocycle is optionally substituted at one or more positions with alkyl (e.g., methyl), alkoxyl(e.g., ethoxy), or halogen (e.g. fluoro).

[0016] Also contemplated are salts of the disclosed compounds including pharmaceutically acceptable salts of the disclosed compounds. Also contemplated are solvates of the disclosed compounds.

[0017] Specifically, the disclosed compounds may have a formula (Ia):

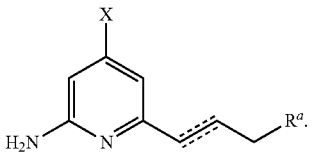
(Ia)



[0018] wherein X, Z, and R^a are as defined above for formula (I) and R^2, R^3, R^4, and R^6, are each independently H or halogen (e.g., fluoro).

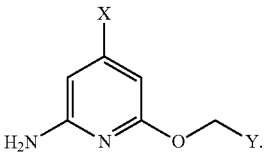
[0019] Specifically, the disclosed compounds may have a formula (Ib)

(Ib)



[0020] specifically, the disclosed compounds may have a formula (II):

(II)



[0021] The disclosed compounds may be formulated as pharmaceutical compositions comprising the compounds or pharmaceutically acceptable salts thereof in a pharmaceutically acceptable carrier for use in treatment methods for a subject in need thereof. In some embodiments, the disclosed compounds and pharmaceutical compositions may be utilized to treat diseases or disorders associated with nitric oxide synthase activity. Particularly, the disclosed compounds and pharmaceutical compositions may be utilized to inhibit nitric oxide synthase in a subject in need thereof and treat diseases or disorders that are associated with nitric oxide synthase activity. In some embodiments, the disclosed compounds and pharmaceutical compositions may be utilized to treat neurological diseases or disorders in a subject in need thereof. Particularly, the disclosed compounds and pharmaceutical compositions may be utilized to treat Alzheimer's, Huntington's and/or Parkinson's disease, amyotrophic lateral sclerosis (ALS), cerebral palsy, and migraine headaches.

BRIEF DESCRIPTION OF THE FIGURES

[0022] FIG. **1**. Structural modifications of compound 1. (i) enhancing rigidity by unsaturated C-C triple bond; (ii) enhancing lipophilicity and rigidity by incorporating pyrrolidine ring; (iii) enhancing lipophilicity by incorporating more fluorine into middle linker; (iv) difluorobenzene linker incorporated with unsaturated C-C triple bond; (v) difluorobenzene linker incorporated with pyrrolidine ring; (vi) modulating pKa of amino tail group.

DETAILED DESCRIPTION

[0023] The present invention is described herein using several definitions, as set forth below and throughout the application.

[0024] Definitions

[0025] The disclosed subject matter may be further described using definitions and terminology as follows. The definitions and terminology used herein are for the purpose of describing particular embodiments only and are not intended to be limiting.

[0026] As used in this specification and the claims, the singular forms "a," "an," and "the" include plural forms